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Leukaemia Section

Short Communication

t(11;16)(q23;p13)

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Clinics and pathology

Disease

ANLL/MDS: only treatment related leukaemias cases so far (in other 11q23 translocations, most cases occur in de novo acute leukaemia).

Phenotype / cell stem origin

M4, M2 ANLL; CMML and RAEBT, although MDS is otherwise rarely seen in 11q23 translocations; the fusion gene is found in all the mature monocytes, in some of the granulocytes and erythroblasts, not in the lymphocytes.

Epidemiology

13 available cases; most cases are children cases: median age is 10-14 yrs, range is 2-74 yrs; sex ratio is balanced.

Clinics

Secondary to antitopoisomerase II drugs (etoposide or teniposide, but also doxorubicin); this secondary malignancy occurs within 6-60 mths (median 20 mths); the primary malignancy was a t(8;21)(q22;q22)/M2-ANLL in 2 cases.

Prognosis

Yet unknown.

Cytogenetics

Additional anomalies

Are found in 8 of 11 cases; variable, except the unexpectected recurrence of 1p36.1 involvement.

Genes involved and Proteins

MLL

Location: 11q23

DNA / RNA

21 exons, spanning over 100 kb; 13-15 kb mRNA.

Protein

431 kDa; contains two DNA binding motifs (a AT hook, and Zinc fingers), a DNA methyl transferase motif, a bromodomain; transcriptional regulatory factor; nuclear localisation.

CBP

Location: 16p13

Protein

Nuclear localisation; transcriptional adaptor/coactivator: binds CREB; has histone acetyltransferase activity.

Results of the chromosomal anomaly

Hybrid gene

Description

5' MLL - 3' CBP

Fusion protein

Description

N-term AT hook and DNA methyltransferase from MLL fused to most of CBP starting with the bromodomain of CBP -or even more in N-term with the CREB binding domain- and also comprising the cystein/histidine rich and the glutamine rich domains of CBP in C-term around 1400 amino acids from MLL; the reciprocal CBP-MLL may or may not be expressed.

Oncogenesis

May promote histone acetylation of genomic regions targeted by the MLL AT-hooks; may loose CBP cell cycle inhibition capability.

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